Summary of risk management plan for Methylthioninium chloride Cosmo (methylthioninium chloride)

This is a summary of the risk management plan (RMP) for Methylthioninium chloride Cosmo. The RMP details important risks of Methylthioninium chloride Cosmo, how these risks can be minimised, and how more information will be obtained about Methylthioninium chloride Cosmo's risks and uncertainties (missing information).

Methylthioninium chloride Cosmo's summary of product characteristics (SmPC) and its package leaflet give essential information to healthcare professionals and patients on how Methylthioninium chloride Cosmo should be used.

This summary of the RMP for Methylthioninium chloride Cosmo should be read in the context of all this information including the assessment report of the evaluation and its plain-language summary, all of which is part of the European Public Assessment Report (EPAR).

Important new concerns or changes to the current ones will be included in updates of Methylthioninium chloride Cosmo's RMP.

I. The medicine and what it is used for

Methylthioninium chloride Cosmo® is authorised to aid the detection and visualisation of colon lesions during colonoscopy (see SmPC for the full indication). It contains methylthioninium chloride as the active substance and it is given by tablets administered orally along with a standard bowel cleansing preparation, prior to colonoscopy.

Further information about the evaluation of Methylthioninium chloride Cosmo's benefits can be found in Methylthioninium chloride Cosmo's EPAR, including in its plain-language summary, available on the EMA website https://www.ema.europa.eu/en/medicines/human/EPAR/methylthioninium-chloride-cosmo.

II. Risks associated with the medicine and activities to minimise or further characterise the risks

Important risks of Methylthioninium chloride Cosmo, together with measures to minimise such risks and the proposed studies for learning more about Methylthioninium chloride Cosmo's risks, are outlined below.

Measures to minimise the risks identified for medicinal products can be:

- Specific information, such as warnings, precautions, and advice on correct use, in the package leaflet and SmPC addressed to patients and healthcare professionals;
- Important advice on the medicine's packaging;
- The authorised pack size — the amount of medicine in a pack is chosen so to ensure that the medicine is used correctly;
- The medicine's legal status — the way a medicine is supplied to the patient (e.g. with or without prescription) can help to minimise its risks.

Together, these measures constitute *routine risk minimisation* measures.

II.A List of important risks and missing information

Important risks of Methylthioninium chloride Cosmo are risks that need special risk management activities to further investigate or minimise the risk, so that the medicinal product can be safely taken. Important risks can be regarded as identified or potential. Identified risks are concerns for which there is sufficient proof of a link with the use of Methylthioninium chloride Cosmo. Potential risks are concerns for which an association with the use of this medicine is possible based on available data, but this association has not been established yet and needs further evaluation. Missing information refers to information on the safety of the medicinal product that is currently missing and needs to be collected (e.g. on the long-term use of the medicine);

Summary of safety concerns	
Important identified risks	• None
Important potential risks	• Serotonin syndrome • Reproductive toxicity
Missing information	• Use in patients with cardiovascular disease • Use in patients with gastrointestinal disease

II.B Summary of important risks

Important Potential risk 1 - Serotonin syndrome	
Evidence for linking the risk to the medicine	Serotonin syndrome has been reported with the use of methylthioninium chloride / methylthioninium chloride class products.
Risk factors and risk groups	Patients who are co-administered methylthioninium chloride when receiving serotonergic psychiatric drug.
Risk minimisation measures	Routine risk minimisation measures: Section 4.4 and 4.5 states that patients who are administered serotonergic drugs may experience serotonin syndrome. Additional risk minimisation measures None

Important Potential risk 2- Reproductive toxicity	
Evidence for linking the risk to the medicine	Intra-amniotic injection of pregnant women with a methylthioninium chloride class product during the second trimester was associated with neonatal intestinal atresia and foetal death. Intra-amniotic or IV injection of a methylthioninium chloride class product hours to days before birth can result in hyperbilirubinemia, haemolytic anaemia, skin staining, methaemoglobinaemia, respiratory distress and photosensitivity in the new born
Risk factors and risk groups	Pregnant and breast feeding women
Risk minimisation measures	Routine risk minimisation measures: It is recommended in Section 4.3 and 4.6 that methylthioninium chloride is not used during pregnancy and breastfeeding should be

Important Potential risk 2- Reproductive toxicity	
	discontinued prior to and after treatment with Methylthioninium chloride Cosmo. Additional risk minimisation measures None

Missing information 1:– Use in patients with cardiovascular disease	
Risk minimisation measures	Routine risk minimisation measures: None Additional risk minimisation measures None

Missing information 2: Use in patients with gastrointestinal disease	
Risk minimisation measures	Routine risk minimisation measures: None Additional risk minimisation measures None